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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61B 17/00

A1

(11) International Publication Number: WO 00/18301

(43) International Publication Date: 6 April 2000 (06.04.00)

(21) International Application Number: PCT/US99/21744

(22) International Filing Date: 21 September 1999 (21.09.99)

(30) Priority Data:
09/161,193 25 September 1998 (25.09.98) US

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(81) Designated States: CA, IL, JP, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.

(54) Title: BIOLOGICAL SEALANT MIXTURE AND SYSTEM FOR USE IN PERCUTANEOUS OCCLUSION OF PUNCTURE SITES AND TRACTS IN THE HUMAN BODY AND METHOD

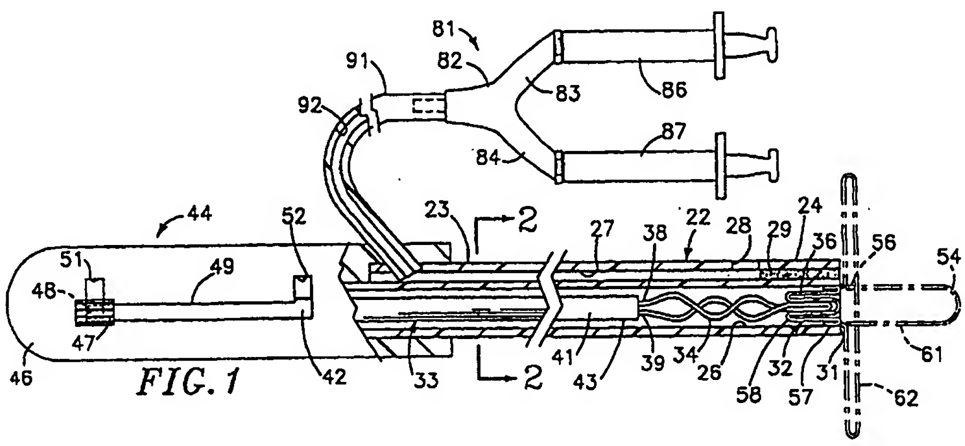

FIG. 1

(57) Abstract

A closure device (21) comprises a tubular member (22) which is coupled to a deployment mechanism (33), a coil (34) having a plurality of circular turns (37), a push/pull wire (41) which is slidable disposed in a main lumen (26), and a handle assembly (44). The closure device (21) further includes a gelatin slurry (723).

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BIOLOGICAL SEALANT MIXTURE AND SYSTEM FOR USE IN PERCUTANEOUS OCCLUSION OF PUNCTURE SITES AND TRACTS IN THE HUMAN BODY AND METHOD

This invention relates to an expansile device for use in vascular and non-vascular tracts in the human body and method and more particularly for percutaneous occlusion of vascular access sites in the human body.

Percutaneous access to the blood vessels and organs of the human body for diagnosis and treatment of disease processes has heretofore been accomplished. Percutaneous vascular procedures are performed involving the coronary, peripheral and cerebral vasculature. These procedures include coronary and peripheral angiography, angioplasty, atherectomies, coronary retroperfusion and retroinfusion, cerebral angiograms, treatment of strokes, cerebral aneurysms and the like. Patients undergoing such procedures are often treated with anti-platelet drugs, anticoagulants such as heparin, thrombolytics, or a combination thereof, all of which interfere with coagulation making it more difficult for the body to seal a puncture site. Various devices and methods have heretofore been utilized, however, they all have had deficiencies, including the use of complicated devices and methods. In addition, difficulties are still encountered in obtaining good seals. There is therefore a need for a device and method for percutaneous access and occlusion of vascular access sites and other puncture sites and

natural tracts in the human body which overcome the deficiencies of prior art devices and methods.

In general, it is an object of the present invention to provide a closure device and method for percutaneous access and occlusion of vascular access sites, other puncture sites and natural tracts in the human body which will make possible a positive seal of the puncture site or tract promoting rapid healing of the puncture site or tract.

Another object of the invention is to provide a closure device and method of the above character which can be easily and reliably used.

Another object of the invention is to provide a biological sealant in the form of a gelatin slurry containing saline, thrombin and calcium.

Another object of the invention is to provide a biological sealant in the form of a Gelfoam® slurry containing saline, thrombin and calcium.

Another object of the invention is to provide a process for making a gelatin slurry biological sealant.

Another object of the invention is to provide a system and method for using a gelatin slurry biological sealant in conjunction with other vascular closure devices.

Additional objects and features of the invention will appear from the following description in which the preferred embodiments and the methods using the same are described in conjunction with the accompanying drawings.

Figure 1 is a side-elevational view partially in section of a closure device for obtaining percutaneous access and occlusion of puncture sites in the human

body incorporating the present invention and having closure means in a de-deployed or retracted position.

Figure 2 is a cross-sectional view taken along the line 2-2 of Figure 1.

Figure 3 is a side-elevational isometric view of the distal end of the device shown in Figure 1 with the closure means in a deployed or extended position.

Figure 4 is a cross-sectional view taken along the line 4-4 of Figure 3 and shows the manner in which a seal is formed with respect to a puncture.

Figures 5A-5D are cartoons demonstrating the method of using the device of the present invention for occluding a vascular access or puncture site.

Figure 37 is an isometric view of an injection sheath contained in the biological sealant system incorporating the present invention.

Figure 38 is a cross section view taken along the line 38-38 of Figure 37.

Figures 39A-C are cartoons demonstrating the biological sealant system and method of using a gelatin slurry biological sealant in conjunction with a vascular closure device utilizing sutures to occlude a puncture.

Figures 40A-C are cartoons demonstrating the biological sealant system and method of using a gelatin slurry biological sealant in conjunction with a vascular closure device utilizing an anchor, hemostatic plug and sutures to occlude a puncture.

Figures 41A-E are cartoons demonstrating the biological sealant system and method of using a gelatin slurry biological sealant in conjunction with a

vascular closure device utilizing an insertion sheath and a mass of hemostatic material disposed therein.

In general, the closure device of the present invention is used for the percutaneous occlusion of a puncture site and natural tract in the human body. The human body has an outer layer of skin and inner layers of tissue surrounding a blood vessel having a lumen therein defined by a vessel wall. A puncture site traverses these layers and, in the case of a vascular access puncture, the vessel wall. The closure device comprises a flexible elongate tubular member having proximal and distal extremities, an outer diameter and extending along a longitudinal axis. The flexible elongate tubular member has a first lumen extending therethrough from the proximal extremity to the distal extremity. A closure assembly is carried by the distal extremity and includes a closure mechanism and an impermeable membrane at least partially covering the closure mechanism. Deployment means carried by the proximal extremity of the flexible elongate tubular member are adapted to be operated by the human hand. The deployment means extends through the flexible elongate tubular member, includes a push-pull wire and is coupled to the closure assembly for moving the closure assembly from a de-deployed or contracted position for introduction into and through a puncture to a deployed position for forming a seal occluding the puncture.

More specifically, as shown in Figures 1-4, the closure device 21 of the present invention for percutaneous occlusion of puncture sites and natural tracts consists of a flexible elongate tubular member

22 formed of a suitable plastic material such as polyethylene or polyurethane or polyimide. The flexible elongate tubular member 22 has a longitudinal axis and proximal and distal extremities 23 and 24. The flexible elongate tubular member 22 is provided with a main circular in cross-section first lumen 26 which may be centrally disposed extending from the proximal extremity 23 to the distal extremity 24. It is also provided with an additional or second lumen 27 which may be crescent-shaped as shown in cross-section in Figure 2 extending from the proximal extremity 23 to the distal extremity 24 where it opens through an external port 28. A plug 29 of a suitable material such as plastic is placed in the lumen 27 to occlude the lumen 27 distal of the port 28.

The flexible elongate tubular member 22 is of a suitable size, as for example a diameter ranging from 1-9 French corresponding to an outside diameter ranging from approximately .3 to 3.0 millimeters. The flexible elongate tubular member has a suitable length as for example 15-30 centimeters with the external port 28 being disposed a suitable distance adjacent to and proximal of the closure assembly 32, as for example from 1-10 millimeters up to several centimeters. The first lumen 26 may have an inside diameter ranging from .015" to 0.080", preferably .020"-.030" while the second lumen 27, if crescent-shaped may have a long axis dimension of approximately 0.015" to 0.080".

Closure means in the form of a closure assembly 32 is carried by the distal extremity 24 of the flexible elongate tubular member 22 and is coupled or secured to deployment means or mechanism 33 for movement from a

contracted, retracted or de-deployed position to an expanded or deployed position. The closure assembly 32 includes a closure mechanism 34 and an impervious membrane 36 which covers the closure mechanism 34. The closure mechanism 34 as shown in Figures 3 and 4 is in the form of a complex geometrical configuration, as for example a coil, when in a free state. The coil 34 is formed of a suitable material which can be elongated without permanent deformation but when freed or unconstrained has a substantial portion thereof which will return to a generally planar or disk-like configuration to which it has been annealed. One material found to be particularly suitable for such an application is a super-elastic or shape memory element as formed of a nickel/titanium alloy, often called Nitinol. The coil 34 has a plurality of generally circular turns 37 and has first and second ends 38 and 39 secured to the deployment mechanism 33 in a manner hereinafter described. The turns 37 of the coil 34 lie in a single plane which is generally perpendicular to the longitudinal axis of the flexible elongate tubular member 22.

The coil 34 has a diameter which is selected to overlap a puncture site as hereinafter described to occlude the puncture site. Typically, a suitable diameter such as 3 to 7 millimeters and preferably approximately 5 millimeters is used. In the de-deployed configuration the constrained coil 34 has a suitable diameter ranging from .1 mm to 3.0 mm. The coil 34 can be formed of wire having a diameter ranging from 0.002" to 0.004" (.05 to .1 millimeters) and preferably about 0.003" (.076 millimeters).

Alternatively, it can be formed of ribbon generally rectangular in cross-section and can have a thickness of approximately 0.001" to 0.002" (.025 to .05 mm.) and a width of approximately 0.003" to 0.005" (.076 to .13 millimeters).

The deployment means or mechanism 33 consists of a push-pull wire 41 which is slidably disposed in and extending through the first or main lumen 26 and has proximal and distal extremities 42 and 43. The push-pull wire 41 is formed of a suitable material such as stainless steel and has a suitable diameter as for example 0.005" to 0.032". Means is provided for securing the two ends 38 and 39 of the coil 34 to the distal extremity 43 of the push-pull wire 41 and consists of solder forming joints or adhesively bonded joints. As shown in Figure 1 the proximal end 42 of the push-pull wire 41 extends out of the proximal extremity 23 of the flexible elongate tubular member 22 and is operatively connected to a handle assembly 44 as hereinafter described.

The handle assembly 44 is formed of a body 46 of suitable material such as plastic and is mounted on the proximal extremity 23 of the flexible elongate tubular member 22. The handle 44 is sized so it is adapted to be grasped by the human hand and is provided with means for operation of the push-pull wire 41 which includes a button 47 adapted to be engaged by a finger of the hand holding the handle. The button 47 is mounted on a protrusion 48 which is slidably mounted in a longitudinally extending slot 49 in the handle 44 and is movable between first and second positions for deploying the coil 34 from a retracted or contracted

elongate position constrained within the flexible elongate tubular member 22 to an expanded position outside of the tubular member 22. The proximal extremity 42 of the push-pull wire 41 is secured to the protrusion 48 in a suitable manner such as a wire clamp or adhesive (not shown). The slot 49 opens into sideways extending notches 51 and 52 provided in the body which can receive the protrusion 48 in either the first or second position to retain the push-pull wire 41 in the desired position as hereinafter described.

The closure means 32 also includes a flexible impermeable membrane 36 which is carried by and secured to the distal extremity 24 of the flexible elongate tubular member 22. It is desired that this membrane 36 be very flexible and it therefore has a wall thickness ranging from 0.0005" to 0.010" (.0127 to .076 millimeters) and preferably 0.001" (.025 millimeters). It can be formed of any suitable flexible impermeable material such as elastomeric and non-elastomeric materials. For example, latex or silicone have been found to be suitable. The membrane 36 should be substantially impermeable to blood and other liquids. It is preferably formed as a tubular sock which can have an elongate generally cylindrical configuration with one closed end 54 and the other end circumscribed by an opening 56 which is defined by a rim 57 of the impermeable membrane. This rim 57 is circumferentially secured to the distal extremity 24 in a suitable manner such as by an adhesive (not shown) and preferably interiorly within the first or main lumen 26. However, if desired, the rim 57 can also be affixed exteriorly to the outer surface of the tip 31 of the distal

extremity 24 of the flexible elongate tubular member 22. The impermeable membrane 36 is formed in such a manner so that it can, upon manufacture of the device 21, be disposed internally of the distal extremity 24 of the flexible elongate tubular member 22 and be folded inwardly with folds 58 in the main lumen 26 to accommodate closure mechanism 34 in a constrained, retracted or contracted or de-deployed position as shown in Figure 1. It also has the flexibility of being moved outwardly by operation of the push-pull wire 41 to the sock-like dotted line position 61 shown in Figure 1.

The impermeable membrane 36 also can be caused to assume a disk-like planar configuration as shown by the dotted-line position 62 in Figure 1. This is accomplished by operation of the deployment mechanism 33 to move the push-pull wire 41 distally to urge the closure mechanism 34 distally to move out of the lumen 26 into the dotted-line position 61. As soon as the closure mechanism 34 is clear of the main lumen 26, it will expand into its memorized configuration. As this expansion is occurring, the membrane 36 covering the coil 34 is caused to move from the sock-like configuration 61 to the disk-like circular configuration 62 so that the membrane 36 is disposed on opposite sides of the closure mechanism 34 and lies in generally parallel planes which are generally perpendicular to the longitudinal axis of the flexible elongate tubular member 22 for percutaneously occluding a puncture as hereinafter described. The deployed closure mechanism 34 is sufficiently rigid so as to provide a supporting framework for the membrane 36.

The closure device 21 also consists of biological sealant introducer means 81 carried by the handle 44 and the flexible elongate tubular member 22 for introducing a biological sealant into a puncture proximal of the closure assembly 32 after the closure assembly 32 has been positioned. The biological sealant is of a suitable type such as a two-component fibrin glue, thrombin, fibrin, collagen-thrombin, collagen, Avitene (trademark), Gelfoam (trademark), cellulose, gelatin, and mixtures or slurries thereof.

One such mixture which assists hemostasis comprises a gelatin slurry. The slurry is made, preferably under sterile conditions and at room temperature, by the process of mixing gelatin powder with saline or water, preferably adding thrombin powder and calcium ions. A buffer may also be added to the solution. The mixture is blended to obtain a homogenous slurry which demonstrates superior flow characteristics in that it exhibits minimal dilatency in comparison to Avitene® and other collagen mixtures. This quality provides a hemostatic agent which can be easily injected or introduced through catheter lumens, especially small lumens.

More specifically, Gelfoam® powder is commercially available from Pharmacia & Upjohn. It is a heat-sterilized, water-insoluble, non-elastic, porous, pliable fine gelatin powder obtained from milling absorbable gelatin sponge which has been derived from purified porcine skin. The slurry of the present invention is obtained by blending Gelfoam powder with saline to obtain a .5-20 per cent solution by weight. Thrombin powder is added in the amount ranging from 1-

20,000 units per milliliter of solution, preferably, 1,000 units per milliliter of solution. Preferably, calcium is added in the form of calcium gluconate, calcium chloride, calcium citrate or any other suitable calcium preparation in which case the slurry can be buffered. A calcium ion concentration ranging from approximately 1-500 milli-moles per milliliter of liquid is obtained. Preferably, a concentration of 8 milli-moles per milliliter is obtained by adding calcium chloride.

The ingredients for the gelatin slurry can be provided in a sterilely pre-packaged biological sealant system or kit. The system comprises a pre-determined quantity of Gelfoam powder packed in a first syringe which can be connected to a first female fitting of a three-way stopcock and a predetermined quantity of thrombin powder placed in a second syringe which can be connected to a second female fitting, preferably both Luer fittings, of the three-way stopcock. A sterile vial is also provided and includes a predetermined quantity of saline or water diluent with or without a predetermined quantity of calcium gluconate or calcium chloride. Accordingly, during a percutaneous vascular puncture closure procedure, when the operator is ready to inject the biological sealant, the system is opened under sterile conditions. The Gelfoam slurry is blended by, preferably, first adding the contents of the vial to the syringe containing the thrombin. Next, the two syringes are connected to the three-way stopcock and, by directing the three-way stopcock into a position wherein the two pre-loaded syringes are in communication with one another, the thrombin solution

is injected into the syringe containing the Gelfoam. The mixture created thereby is then injected back into the empty syringe. The repeated, alternating deployment of the syringe plungers easily and effectively blends the contents of the two syringes to create a homogenous Gelfoam-thrombin slurry which can be deposited in one of the syringes. The kit or system can also include a modified injection catheter 701 for use in conjunction with other vascular closure devices. The catheter 701, shown in Figure 37, is a conventional catheter made of a suitable material such as plastic and having a diameter ranging from 3-10 French and a length ranging from 2-10 inches. As shown in Figures 37-38, the distal end of the catheter 701 carries a longitudinal slit or slot 702 which extends proximally a variable distance from the distal-most tip of the catheter 701. As shown in Figure the slit 702 carries a bevel 703 directed towards a lumen 704 in the catheter 701. The proximal end of the slit 702 in the catheter 701 is provided with an enlarged portion, or eye 706. It should be appreciated that the entire length of the catheter 701 can be slit. As hereinafter described, this system facilitates introduction of the Gelfoam slurry when used with other vascular closure devices.

It should be appreciated that other biological sealants or pharmacological agents may also be introduced into a puncture utilizing this device.

The biological sealant introducer means 81 can consist of a fitting of a suitable type such as a wye adapter 82 which is provided with first and second arms 83 and 84 with first and second syringes 86 and 87

removably mounted thereon on and containing the two separate constituents of fibrin glue being used as the biological sealant. The fitting 82 is connected to a flexible tubular member 91 which is sealed into the handle 44 and is provided with a lumen 92 therein in communication with the lumen (not shown) of the arms 83 and 84. The distal end of the flow passage 92 in the tubular member 91 is aligned to be in communication with the second lumen 27 of the flexible elongate tubular member 22 so that when the syringes 86 and 87 are operated the biological sealant components are mixed and pass through the flow passage 92 existing via the external port 28 of the second lumen 27.

Operation and use of the device 21 in performing the method of the present invention in the percutaneous access and occlusion of vascular access sites and other puncture sites in the human body may now be described in conjunction with the cartoons shown in Figures 5A-5D. Let it be assumed that a percutaneous femoral arterial catheterization is to be performed. After sterile preparation, a thin-walled hollow needle with syringe (not shown) is percutaneously inserted through the skin 101, the underlying subcutaneous tissue 102 and then through the wall 103 defining the lumen 104 of a vessel 107 such as the femoral artery to form a puncture 106. Intra-arterial access is confirmed by the aspiration of arterial blood. A flexible wire (not shown) is then passed through the needle into the artery 107 and the needle is removed, leaving only the wire in place in the puncture 106. A vessel dilator (not shown) with a shorter conventional over-lying sheath 111 is passed over the wire through the puncture

106 into the lumen 104 after which the wire and dilator are removed. The sheath 111 extends from outside the patient through skin 101 and subcutaneous tissues 102 and through the wall 103 into the lumen 104 as shown in Figure 5A. Various diagnostic and therapeutic catheters and other similar medical devices can be passed through the sheath 111, whose diameter can range from 3 to 24 French, to perform desired procedures, as for example an angioplasty procedure during which time anti-coagulants such as heparin have been introduced. At the conclusion of any such procedure, such instruments are removed leaving only the sheath 111 in place.

Let it be assumed that it is now desired to seal the puncture 106. The closure device 21 of the present invention with the closure assembly 32 in the retracted position as shown in Figure 1 is inserted into the sheath 111 while maintaining standard sterile precautions. The distal extremity 24 of the flexible elongate tubular member 22 is passed through the sheath 111 and into the lumen 104 so that it extends a short distance up to several inches beyond the distal extremity of the sheath 111 as shown in Figure 5A. The sheath 111 is then slowly, incrementally withdrawn proximally while maintaining the device 21 as stationary as possible. As can be seen from Figure 5B, the flexible elongate tubular member 22 has a length so that the sheath can be removed from the puncture 106 while retaining the distal extremity 24 in the lumen 104 and without removing the handle 44. When the sheath 111 has been withdrawn as shown in Figure 5B, the closure assembly 32 may be deployed by operation of

the deployment mechanism 33. Alternatively, the distal extremity 24 of the flexible elongate tubular member 22 can be passed into the lumen 104 a slightly greater distance, the device 21 deployed with the sheath 111 still in position, and then both the sheath 111 and device 21 slowly withdrawn so that the sheath 111 is removed from the lumen 104 with the deployed device 21 appropriately positioned in the lumen 104.

Before deployment of the closure assembly 32, the finger button 47 is in its most proximal-most position with the protrusion 48 being seated in the notch 51 as shown in Figure 5A. Now let it be assumed that it is desired to move the closure assembly 32 from a contracted or retracted position where it is disposed within the first main lumen 26. When it is desired to move the closure assembly 32 to an expanded or open position, the button 47 is retracted from the notch 51 and slidably advanced along the slot 49 to push the distal extremity 43 of the push-pull wire 41 distally to cause the Nitinol closure mechanism 34 to be advanced distally and to carry the folded impermeable membrane 36 out of the first or main lumen 26 to cause it to assume a sock-like shape as shown in position 61 in Figure 1. Continued forward movement of the finger button 47 causes further longitudinal movement of the push-pull wire 41 which causes further distal movement of the closure mechanism 33 until it clears the first lumen 26 so that it is substantially free to cause it to expand into its super-elastic or shape memory form of a coil to carry with it the flexible impervious membrane 36 to assume the disk-like configuration represented by position 62 as shown in Figures 1 and 4.

The finger knob is then positioned so that the protrusion 48 is seated in the notch 52.

After the closure mechanism has been fully deployed, the handle 44 can be utilized to gradually retract the flexible elongate member 22 to ensure that the proximal surface of the flattened flexible membrane 36 is brought into close engagement with the inner surface of the wall 103 forming the lumen 104 in which the closure assembly 32 is disposed. This forms a liquid tight seal between the closure assembly 32 and the wall 103 immediately adjacent the puncture 106 which in turn enables accurate and effective deposition of the biological sealant into the puncture 106 as hereinafter described. Such a liquid tight seal is also necessary in connection with the present invention to prevent the leakage of blood through the puncture 106. This serves to prevent blood from interfering with attempts to safely and permanently occlude and seal the puncture 106 and to prevent inadvertent intravascular deposition of sealant.

The formation of a good seal between the occlusion assembly 32 and the wall 103 of the vessel 107 can be ascertained in several ways. By way of example the absence of arterial blood in the puncture 106 serves to verify that a good seal has been made. Attempts to aspirate blood from the second lumen 27 with no blood return therefrom also indicates accurate placement of the device 21. Alternatively, fluoroscopy can be utilized to check the position of the closure assembly 32. This is made possible because of the radio opacity of the closure mechanism 34. Radio opaque dyes may also be utilized to ascertain whether the puncture has

been effectively sealed. A small amount of radio opaque dye may be injected into the subcutaneous tissue adjacent the puncture 106. If fluoroscopy demonstrates intravascular dye then there is inadequate placement of the closure assembly 32. If perchance there is any leakage, the button 47 can be engaged by the finger and retracted out of the notch 52 and proximally for a slight distance and then moved distally to re-deploy the mechanical assembly 32, thereafter grasping the handle 44 and pulling the flexible elongate member 22 proximally to again reestablish a seal with the wall 103 adjacent the puncture 106.

As soon as it has been established that a good seal has been formed in the manner hereinbefore described between the closure assembly 32 and the wall 103 adjacent the puncture 106, a biological sealant to be utilized can be introduced into the puncture 106 to provide a sealant 116 which extends throughout the puncture 106 from immediately outside the vessel 107 up to as far as the outer surface of the skin 101 as shown in Figure 5C. It should be appreciated, however, that it may not be necessary to introduce an amount of sealant so great as to cause it to extend proximally to the skin. Assuming that the biological sealant is a fibrin glue supplied in two ports in the syringes 86 and 87, the physician utilizing the closure device 21 while holding the handle 44 in one hand utilizes the other hand to operate the syringes 86 and 87 to cause the constituents of the biological sealant to be introduced into the wye adapter 82 where they are mixed with each other and introduced through the tubular member 91 and into the second lumen 27, thence through

the exit port 28 which is adjacent the closure assembly 32. It should be appreciated that in addition to holding the handle 44 in order to maintain engagement of the closure assembly 32 with the vessel wall 103, any suitable device by way of example a pin-vise may be applied to the flexible elongate tubular member 22 immediately adjacent the skin 101 so that the engagement is maintained and the physician has a free hand. The fibrin glue seals the innermost tissue layers in the puncture 106 and then, as hereinbefore described, can backfill the puncture 106 through the subcutaneous tissue 102 and to the skin 101, surrounding the distal extremity 24 of the flexible elongate tubular member 21 as shown in Figure 5C. If necessary, the completion of this backfilling can be observed by the fibrin glue exiting from the puncture 106. As soon as this occurs, the physician terminates further movement of the syringes 86 and 87 and then while still holding the handle 44 to retain the closure assembly 32 in place, permits the fibrin glue to set up or cure within the puncture 106 for a period of time suitable to permit the fibrin glue to form a sticky adherent clot in the puncture 106 but to prevent the fibrin glue forming a clot which is too firm so as to preclude easy withdrawal of the closure device 21. Typically this ranges from a period of time of 30 seconds to 15 minutes and preferably a period of time of approximately 1-2 minutes. The aforementioned biological sealants only adhere to collagen-containing tissues which prevents them from bonding to the flexible elongate tubular member 22. As soon as the physician determines that the fibrin glue has assumed

the desired state, the button 47 carried by the handle 44 is engaged by the finger of the physician's hand and moved out of the slot 52 and then retracted proximally in the slot 49 to cause proximal movement of the push-pull wire 41 to cause a gradual straightening of the closure mechanism 34 to bring it substantially within the interior of the lumen 26 thereby permitting collapse of the flexible membrane 36 so that it can assume a generally sock-like configuration. Thus as soon as the button 47 has been moved to its most proximal position and moved into the notch 51, the closure device 21 can gently be pulled from the seal 116 provided in the puncture 107. The hole (not shown) left in the sealant 116 after withdrawal of the flexible elongate tubular member 22 and the membrane 36 carried thereby closes on itself due to the sufficiently gel-like state of the fibrin glue or other agent. Thereafter, the site of the puncture 106 is observed to ascertain whether or not bleeding is occurring therefrom. An excellent biological seal is formed with nothing remaining at the puncture site except for the biological sealant which within a relatively short period of time as for example 1-2 weeks will be absorbed by the body.

From the foregoing it can be seen that there has been provided a closure device and a method for utilizing the same which makes it possible to quickly and efficaciously close the puncture which has been made necessary for performing a desired medical procedure as for example an angioplasty procedure. An excellent seal is formed even though anticoagulants have been introduced into the blood of the patient

during the procedure to prevent the formation of clot. The application of fibrin glue in this manner permits the formation of a good clot to seal the puncture without danger of re-bleeding occurring.

It also should be appreciated that during this procedure in performing the closure of the puncture site, blood can continue to flow substantially unimpeded through the lumen 104 of the vessel. This lack of obstruction is made possible because of the small size of the distal extremity of the closure device 21 and also because of the small size of the closure assembly 32 carried by the distal extremity 24 of the device 21. When the closure assembly 32 is deployed as hereinbefore described, it has a relatively small diameter in comparison to the size of the lumen into which it is introduced. In addition it has a flat planar configuration which, when brought into engagement with the inner surface of the wall 103, is substantially flush with the inner surface of the wall 103. Even when the closure assembly 32 is being de-deployed it occupies very little space as it is being withdrawn.

As hereinbefore described, it should also be appreciated that the process for making the Gelfoam slurry biological sealant and the sealant system or, simply, the Gelfoam slurry hereinbefore described can be utilized in conjunction with other vascular closure devices. One such device is designated by the trademark PROSTAR and is marketed by Perclose, Inc. of Menlo Park, Calif. By the use of percutaneously inserted needles secured to sutures 721, the device percutaneously sutures a puncture 106 in a blood vessel

wall 103 thereby occluding the puncture 106. The sutures 721 are tied and the tails 722 thereof extend proximally, out of the tissue tract 106 created at the time of the vascular access procedure and thence out of the body. It has been determined that in spite of using the PROSTAR device to seal a puncture, there is often continued bleeding from the puncture. It is, therefore, advantageous to supplement such a closure with gelatin slurry biological sealant. Accordingly, a Gelfoam slurry biological sealant system is provided as hereinbefore described. Use of the system in conjunction with the PROSTAR is as hereinafter described and shown in Figures 39A-C. The tails 722 of the sutures 721 extending proximally out of the body are threaded through the slot 702 in the distal end of the insertion catheter 701 and into the lumen 704 of the catheter 701 by applying pressure on the bevel 703 of the distal slot 702 with the tails 722. The tails 722 are then pulled proximally until they catch and become disposed in the eye 706 of the slot 702, exiting the lumen 704 of the injection catheter 701 thereat as shown in Figure 39. The distal end of the injection catheter 701 is carefully advanced over the sutures 721 distally into and down the tissue tract 106 associated with the sutured puncture 106 until it is adjacent the vessel wall 103 and sutures 721. After blending the Gelfoam slurry sealant 723, the sealant 723 in the syringe 724 is sterilely deposited into the injection catheter 701, in which the suture tails 722 are partially disposed, as the catheter 701 is withdrawn, thus introducing the sealant 723 into the tract 106 proximal to the wall 103 of the blood vessel 107 and

adjacent the tied sutures 721. The sealant 723 is then permitted to facilitate hemostasis for a predetermined period of time as hereinbefore described. Thereafter, the sealant 723 may be retained in the tissue tract 106, wherefrom it is reabsorbed over a period of time, or it may be removed therefrom. The remainder of the procedure is as hereinbefore described.

Another vascular closure device with which the Gelfoam slurry sealant, system and method may be utilized is designated by the trademark ANGIOSEAL, marketed by Sherwood, Davis and Geck of St. Louis, Missouri. The device uses an introducer sheath to place an absorbable anchor 731 into the vessel 107 through the puncture 106 therein. The anchor 731 carries at least one, usually two, sutures 732 secured thereto, the sutures 732 being adapted to extend from the puncture 106 to outside the body along the tissue tract 106 associated therewith. During deployment, after the anchor 731 is placed intravascularly but before the sheath is removed from the tissue tract 106, a collagen plug 733 or sponge with a hole or lumen which has been threaded over the sutures 732 and engaged thereby is also deposited into the tissue tract 106. The suture 732 is adapted to be pulled proximally by the operator in order to pull the anchor 731 proximally into engagement with the wall 103 in the lumen 104 of the blood vessel 107 whereupon the sutures 732 are ligated over the collagen plug 733. Ligation pulls the collagen plug 733 distally so that it becomes firmly disposed adjacent the outer wall 103 of the vessel 107 and the sutures 732 thereby substantially occluding the puncture 106. As shown in Figures 40A-C,

the remainder of the method of introducing the Gelfoam slurry sealant 723 is as hereinbefore described in conjunction with the PROSTAR device.

Another vascular closure device with which the Gelfoam slurry sealant, system and method may be utilized is designated by the trademark VASCULAR SOLUTIONS DUETT and is marketed by Vascular Solutions of Minneapolis, MN. The device is inserted through a conventional sheath introducer carrying a sidearm and comprises an elongate tubular member having proximal and distal extremities, the distal extremity being sized so that it is adapted to extend through the puncture in the wall into the lumen of the blood vessel, an inflatable member carried by the distal extremity and movable between deflated and inflated positions and deployment means carried by the proximal extremity of the elongate tubular member and adapted to be operated by the human hand for controlling movement of the inflatable member between deflated and inflated positions by the introduction of liquid or air thereto. The method of use of the device and gelatin slurry sealant is as hereinbefore described in conjunction with the vascular closure device of the present invention with the exception that the Gelfoam slurry is introduced through the sidearm of the sheath introducer after the device has been deployed and the distal end of the sheath has been withdrawn proximally out of the vessel.

A variation of the VASCULAR SOLUTIONS DUETT device carries a sealant injection lumen. Use of this device with the gelatin slurry of the present invention is as

hereinbefore described in conjunction with the closure device of the present invention.

Another vascular closure device with which the Gelfoam slurry sealant, system and method may be utilized is designated by the trademark VASOSEAL and is marketed by Datascope. As shown in Figure 41A-E, the device comprises an insertion sheath 751 adapted to be passed distally through a tissue tract 106 until it is adjacent the puncture 106 outside the wall 103 of the vessel 107, a mass of hemostatic material 752, such as a collagen plug, adapted to be disposed in said insertion sheath 751 and means 753 for advancing said hemostatic material 752 distally out of said sheath 751 when said sheath 751 is pulled proximally while manual pressure 754 is maintained on the vessel 107 distal to the puncture 106 so that said hemostatic material 752 is deposited adjacent the puncture 106 outside the wall 103 of the vessel 107 thereby occluding the puncture 106. As shown in Figures 41A-E, the Gelfoam slurry sealant 723, and system for making the same, can be utilized in conjunction with this device by blending the slurry 723 and introducing it into the introducer 751, as hereinbefore described, prior to placing the hemostatic material 752 into the introducer 751.

A variation of the aforementioned devices includes a system marketed by Kensey Nash Corporation of Exton, Pennsylvania. This system comprises the use of the PROSTAR device followed by the insertion of a hemostatic plug which is formed with a lumen through which the suture tails can be extended so that, subsequently, the plug can be threaded distally into the tissue tract in a manner similar to that

hereinbefore discussed. It should be appreciated that the Gelfoam slurry sealant, system and method of using is readily adaptable to this system.

As hereinbefore described, the system of the present invention is also readily adaptable to be used in conjunction with other vascular closure devices.

Percutaneous methods are widespread techniques that offer less invasive, safer and more cost-effective diagnostic and therapeutic access to organs of the human body. The device and method of the present invention obviate many of the morbid side effects associated with puncture sites hereinbefore described.

WHAT IS CLAIMED:

1. A biological sealant comprising a gelatin slurry.

2. A biological sealant as in Claim 1 wherein said slurry includes Gelfoam (trademark) powder mixed with a diluent selected from the group consisting of saline and water.

3. A biological sealant as in Claim 2 wherein said slurry includes gelatin in an amount ranging from .5-10 per cent by weight.

4. A biological sealant as in Claim 3 further including thrombin.

5. A biological sealant as in Claim 4 wherein said slurry includes thrombin in the amount ranging from 10-20,000 units per milliliter.

6. A biological sealant as in Claim 4 further including calcium.

7. A biological sealant as in Claim 6 wherein said slurry includes calcium ions in an amount ranging from 1-500 milli-moles per milliliter of liquid.

8. A process for making a biological sealant for use in percutaneous occlusion of vascular puncture sites comprising the steps of weighing an amount of gelatin powder, mixing said amount of gelatin powder with saline in a ratio of 5-100 mg of gelatin powder per milliliter of saline and blending said gelatin powder and saline together until a homogeneous slurry is created.

9. The process of Claim 8 further including the step of mixing thrombin powder with the gelatin powder and saline in the ratio of 1-20,000 units of thrombin powder per milliter of saline and blending said

thrombin powder with said gelatin powder and saline together until a homogeneous slurry is created.

10. The process of Claim 9 wherein the gelatin powder used is Gelfoam (trademark) powder.

11. The process of Claim 10 further including the step of adding 1-10 millimoles of calcium ion per milliliter of saline to said gelatin powder, saline and thrombin powder

12. A biological sealant for use with a closure device for percutaneously forming a closure of a puncture in a wall of a blood vessel, the closure device having an elongate tubular member having proximal and distal extremities, the distal extremity being sized so that it is adapted to extend through the puncture in the wall, an expansion assembly carried by the distal extremity and movable between contracted and expanded positions and deployment means carried by the proximal extremity of the elongate tubular member and adapted to be operated by the human hand for controlling movement of the expansion assembly between contracted and expanded positions, the biological sealant comprising a gelatin slurry.

13. A biological sealant as in Claim 12 wherein said slurry includes gelatin in an amount ranging from .5-10 per cent by weight.

14. A biological sealant as in Claim 13 wherein said gelatin is Gelfoam (trademark) and the slurry further includes thrombin.

15. A biological sealant as in Claim 14 wherein said slurry includes thrombin in the amount ranging from 1-20,000 units per milliliter.

16. A method for percutaneously forming a closure of a puncture in a wall of a blood vessel in the body, the blood vessel having a lumen defined by the wall, by use of a closure device having an elongate tubular member having proximal and distal extremities, the distal extremity being sized so that it is adapted to extend through the puncture in the wall into the lumen of the blood vessel, an expansion assembly carried by the distal extremity and movable between contracted and expanded positions and deployment means carried by the proximal extremity of the elongate tubular member and adapted to be operated by the human hand for controlling movement of the expansion assembly between contracted and expanded positions and a biological sealant comprising a gelatin slurry, the method comprising introducing the distal extremity of the elongate tubular member and the expansion assembly through the puncture into the lumen of the blood vessel, moving the expansion assembly from a contracted position to an expanded position, pulling the elongate tubular member proximally to bring the expansion assembly into engagement with the wall of the lumen of the vessel, introducing said biological sealant into the body proximal to the wall of the blood vessel and adjacent to the expansion assembly, permitting said biological sealant to assist hemostasis for a predetermined amount of time, thereafter moving the expansion assembly from the expanded position to the contracted position and removing the closure device from the biological sealant.

17. A method as in Claim 16 further including the step of adding thrombin to said biological sealant prior to introducing the sealant into the body.

18. A biological sealant system for use with a closure device for percutaneously forming a closure of a puncture in a wall of a blood vessel in the body, the blood vessel having a lumen defined by the wall, the closure device having an elongate tubular member having proximal and distal extremities, the distal extremity being sized so that it is adapted to extend through the puncture in the wall, an expansion assembly carried by the distal extremity and movable between contracted and expanded positions and deployment means carried by the proximal extremity of the elongate tubular member and adapted to be operated by the human hand for controlling movement of the expansion assembly between contracted and expanded positions, the system comprising a predetermined quantity of gelatin powder, a predetermined quantity of thrombin powder and a predetermined quantity of saline.

19. A system as in Claim 18 wherein said gelatin powder is Gelfoam (trademark) and further including means for mixing said gelatin powder, thrombin powder and saline into a gelatin slurry and introducing said slurry into the body proximal to the wall of the blood vessel and adjacent to the expansion assembly.

20. A system as in Claim 19 wherein said gelatin slurry introducing means includes a syringe.

21. A biological sealant system for use with a closure device for percutaneously forming a closure of a puncture in a wall of a blood vessel in the body, the blood vessel having a lumen defined by the wall, the

closure device having at least one suture adapted to substantially occlude the puncture and to extend from the puncture to outside the body along a tissue tract, the system comprising a predetermined quantity of gelatin powder, a predetermined quantity of thrombin powder and a predetermined quantity of saline.

22. A system as in Claim 21 wherein said gelatin powder is Gelfoam (trademark) and further including means for mixing said gelatin powder, thrombin powder and saline into a gelatin slurry and introducing said slurry into the body into said tissue tract proximal to the wall of the blood vessel and adjacent to the suture.

23. A system as in Claim 22 wherein said gelatin slurry introducing means includes a syringe and an injection catheter having a slit therein.

24. A method for percutaneously forming a closure of a puncture in a wall of a blood vessel in the body, the blood vessel having a lumen defined by the wall, by use of a closure device having at least one suture adapted to substantially occlude the puncture and to extend from the puncture to outside the body along a tissue tract and a biological sealant comprising a gelatin slurry including thrombin, the method comprising suturing the puncture in the wall of the blood vessel with the suture, introducing said biological sealant into the body proximal to the wall of the blood vessel and into said tissue tract adjacent said suture and permitting said biological sealant to assist hemostasis for a predetermined amount of time.

25. A biological sealant system for use with a closure device for percutaneously forming a closure of

a puncture in a wall of a blood vessel in the body, the blood vessel having a lumen defined by the wall, the closure device having an elongate tubular member having proximal and distal extremities, the distal extremity being sized so that it is adapted to extend through the puncture in the wall, an inflatable member carried by the distal extremity and movable between deflated and inflated positions and deployment means carried by the proximal extremity of the elongate tubular member and adapted to be operated by the human hand for controlling movement of the inflatable member between deflated and inflated positions, the system comprising a predetermined quantity of gelatin powder, a predetermined quantity of thrombin powder and a predetermined quantity of saline.

26. A system as in Claim 25 wherein said gelatin powder is Gelfoam (trademark) powder and further including means for mixing said gelatin powder, thrombin powder and saline into a gelatin slurry and introducing said slurry into the body proximal to the wall of the blood vessel and adjacent to the inflatable member.

27. A system as in Claim 26 wherein said gelatin slurry introducing means includes an injection catheter and a syringe.

28. A method for percutaneously forming a closure of a puncture in a wall of a blood vessel in the body, the blood vessel having a lumen defined by the wall, by use of a closure device having an elongate tubular member having proximal and distal extremities, the distal extremity being sized so that it is adapted to extend through the puncture in the wall into the lumen

of the blood vessel, an inflatable member carried by the distal extremity and movable between deflated and inflated positions and deployment means carried by the proximal extremity of the elongate tubular member and adapted to be operated by the human hand for controlling movement of the inflatable member between deflated and inflated positions and a biological sealant comprising a gelatin slurry including thrombin, the method comprising introducing the distal extremity of the elongate tubular member and the inflatable member through the puncture into the lumen of the blood vessel, moving the inflatable member from a deflated position to an inflated position, pulling the elongate tubular member proximally to bring the inflatable member into engagement with the wall of the lumen of the vessel, introducing said biological sealant into the body proximal to the wall of the blood vessel and adjacent to the inflatable member, permitting said biological sealant to assist hemostasis for a predetermined amount of time, thereafter moving the inflatable member from the inflated position to the deflated position and removing the closure device from the biological sealant.

29. A biological sealant system for use with a closure device for percutaneously forming a closure of a puncture in a wall of a blood vessel in the body, the blood vessel having a lumen defined by the wall, the closure device having an absorbable anchor adapted to be placed through the puncture into the vessel, at least one suture secured to said anchor and a hemostatic plug engaging said suture, the suture adapted to extend from the puncture to outside the body

along a tissue tract and to be pulled by the human hand in order to pull the anchor proximally and the hemostatic plug distally in order for said anchor and plug to engage the wall of the blood vessel to substantially occlude the puncture, the system comprising a predetermined quantity of gelatin powder, a predetermined quantity of thrombin powder and a predetermined quantity of saline.

30. A system as in Claim 29 wherein said gelatin powder is Gelfoam (trademark) and further including means for mixing said gelatin powder, thrombin powder and saline into a gelatin slurry and introducing said slurry into the body proximal to the wall of the blood vessel and adjacent to the expansion assembly.

31. A system as in Claim 30 wherein said gelatin slurry introducing means includes an injection catheter having a slit therein and syringe.

32. A method for percutaneously forming a closure of a puncture in a wall of a blood vessel in the body, the blood vessel having a lumen defined by the wall, by use of a closure device having an absorbable anchor adapted to be placed through the puncture into the vessel, at least one suture secured to said anchor and a hemostatic plug engaging said suture, the suture adapted to extend from the puncture to outside the body along a tissue tract and to be pulled by the human hand in order to pull the anchor proximally and the hemostatic plug distally in order for said anchor and plug to engage the wall of the blood vessel to substantially occlude the puncture and a biological sealant comprising a gelatin slurry including thrombin, the method comprising placing the anchor through the

puncture into the vessel, pulling the suture proximally until the anchor and the hemostatic plug engage the wall of the vessel, introducing said biological sealant into the body proximal to the wall of the blood vessel and into said tissue tract adjacent said suture and permitting said biological sealant to assist hemostasis for a predetermined amount of time.

33. A biological sealant system for use with a closure device for percutaneously forming a closure of a puncture in a wall of a blood vessel in the body, the blood vessel having a lumen defined by the wall, the closure device having an insertion sheath adapted to be passed distally through a tissue tract until it is adjacent the puncture outside the wall of the vessel, a mass of hemostatic material adapted to be disposed in said insertion sheath and means for advancing said hemostatic material distally out of said sheath when said sheath is pulled proximally so that said hemostatic material is deposited adjacent the puncture outside the wall of the vessel thereby occluding the puncture, the system comprising a predetermined quantity of gelatin powder, a predetermined quantity of thrombin powder and a predetermined quantity of saline.

34. A system as in Claim 33 wherein said gelatin powder is Gelfoam (trademark) and further including means for mixing said gelatin powder, thrombin powder and saline into a gelatin slurry and introducing said slurry into the body proximal to the wall of the blood vessel and adjacent to the expansion assembly.

35. A system as in Claim 34 wherein said slurry introducing means includes an injection catheter and a syringe.

36. A method for percutaneously forming a closure of a puncture in a wall of a blood vessel in the body, the blood vessel having a lumen defined by the wall, by use of a closure device having an insertion sheath, a mass of hemostatic material adapted to be disposed in said insertion sheath and means for advancing said hemostatic material distally out of said sheath when said sheath is pulled proximally so that said hemostatic material is deposited adjacent the puncture outside the wall of the vessel thereby occluding the puncture and a biological sealant comprising a gelatin slurry including thrombin, the method comprising passing said insertion sheath distally through a tissue tract until is disposed adjacent the puncture outside the wall of the vessel, introducing said biological sealant into the insertion sheath distally so that it flows distally in the sheath and is deposited adjacent the puncture outside the wall of the vessel thereby sealing the puncture, inserting said mass of hemostatic material into the insertion sheath and advancing said hemostatic material distally in said sheath, pulling said sheath proximally while further advancing said hemostatic material distally out of said sheath so that said hemostatic material is deposited adjacent the puncture outside of the wall of the vessel and adjacent to said biological sealant and removing the sheath after a predetermined period of time.

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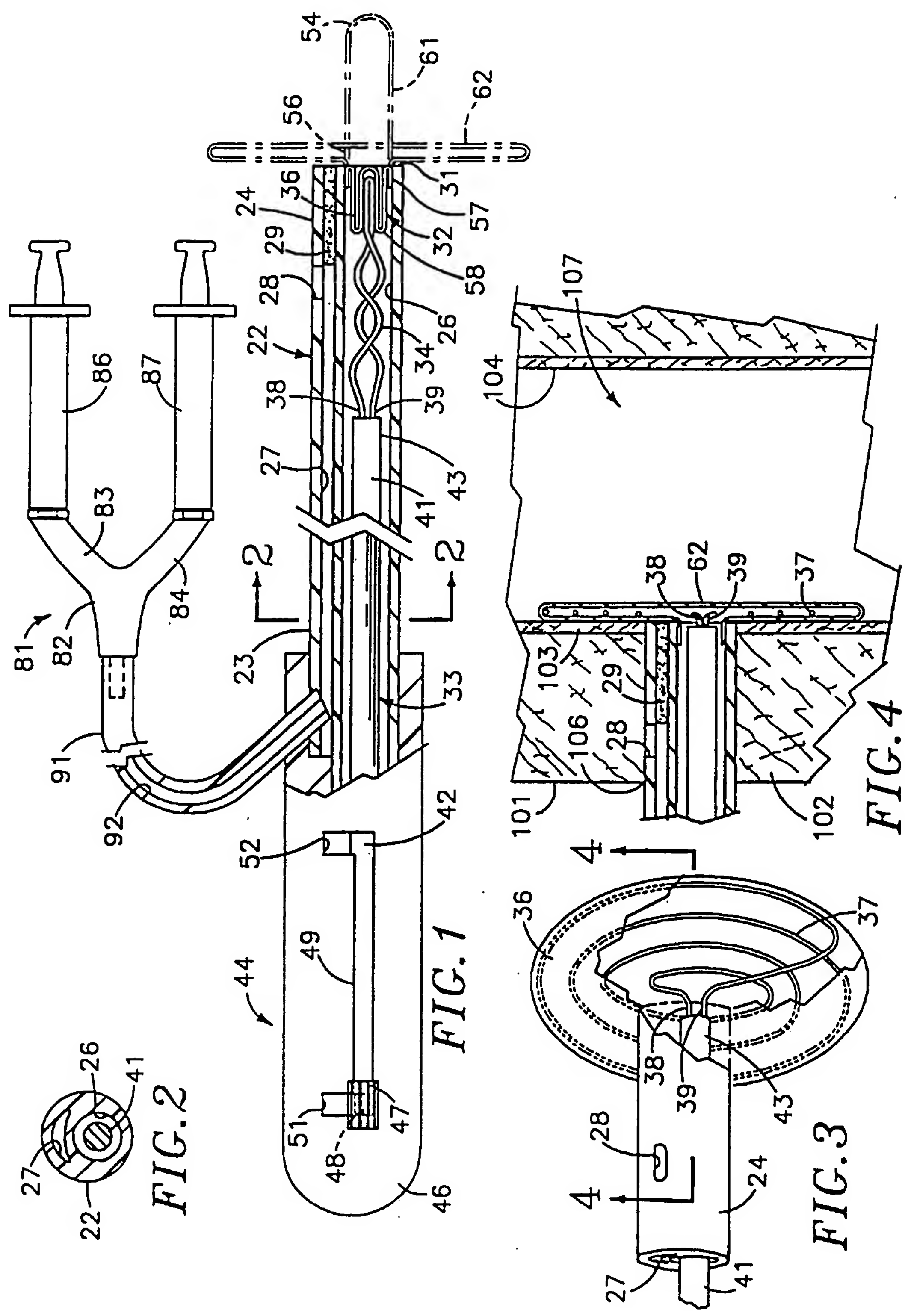

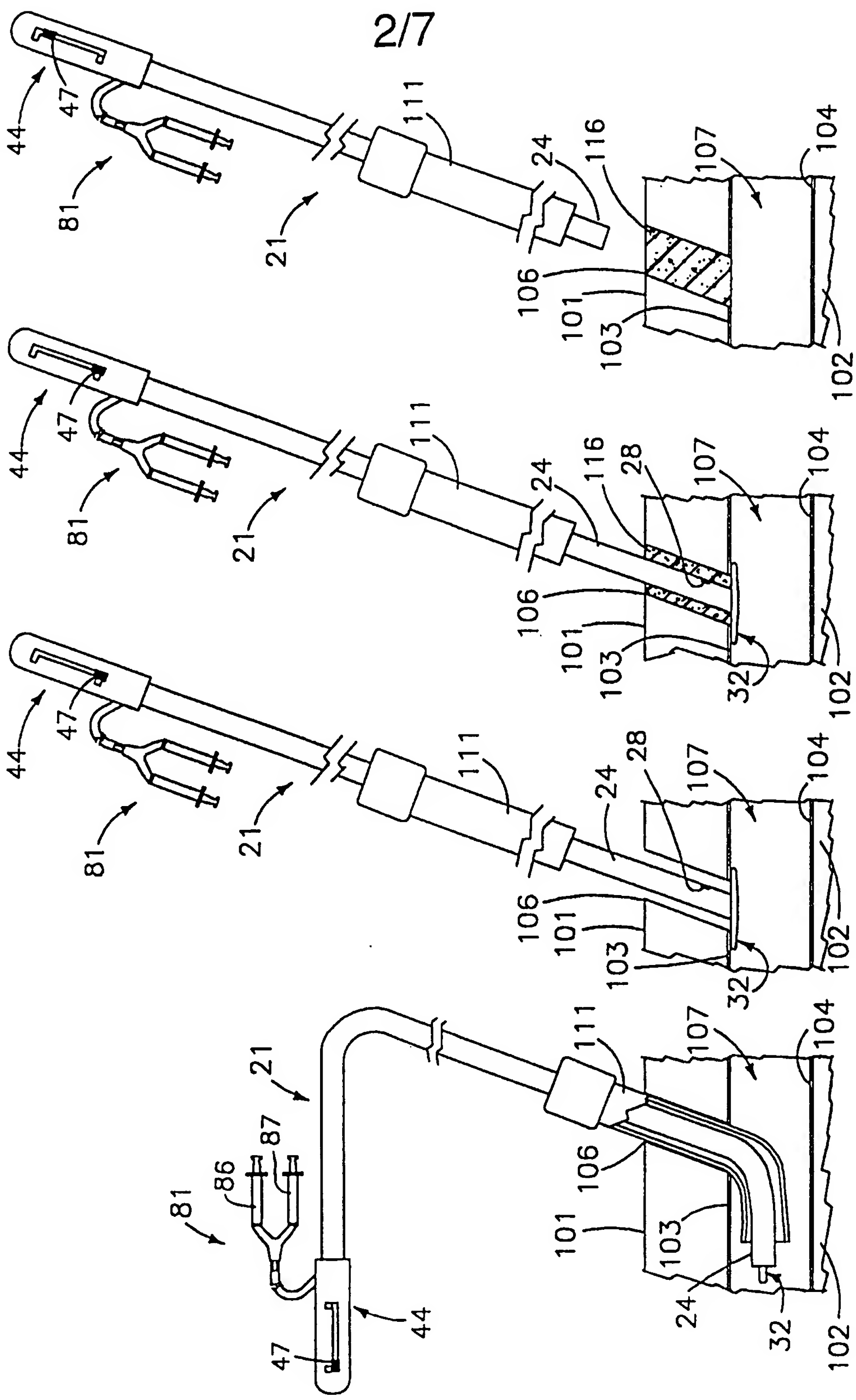

FIG.5A

FIG.5B

FIG.5C

FIG.5D

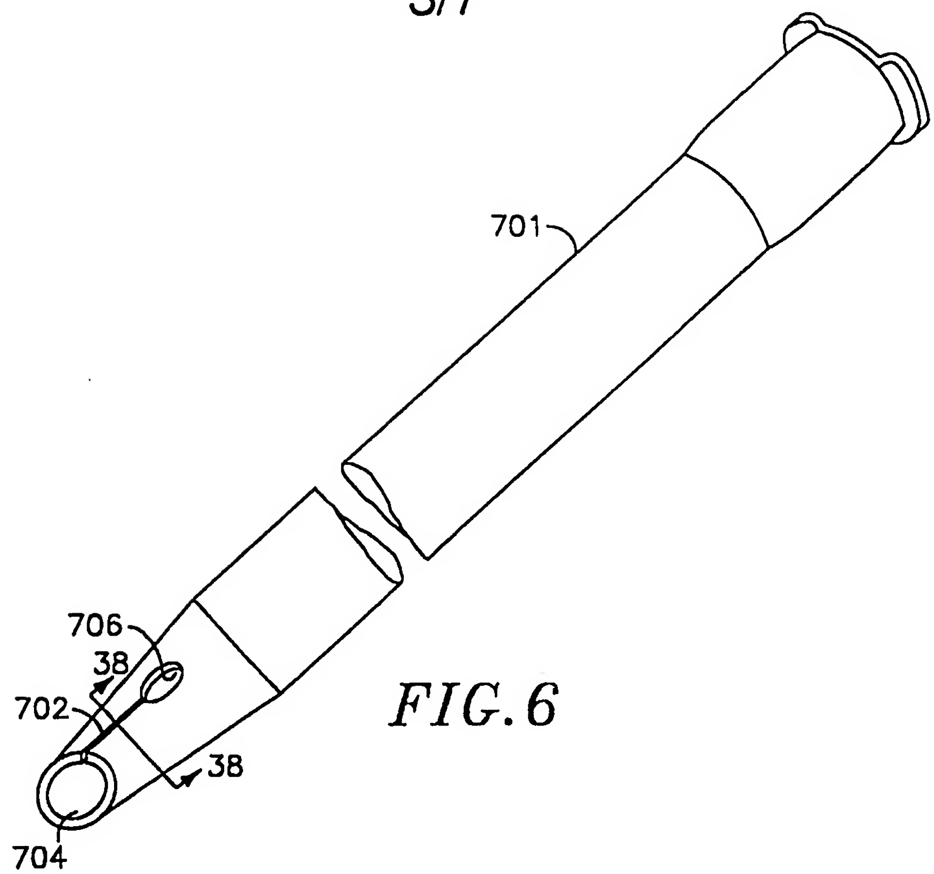

FIG. 6

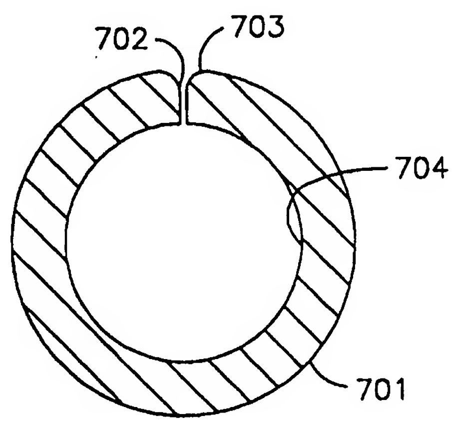

FIG. 7

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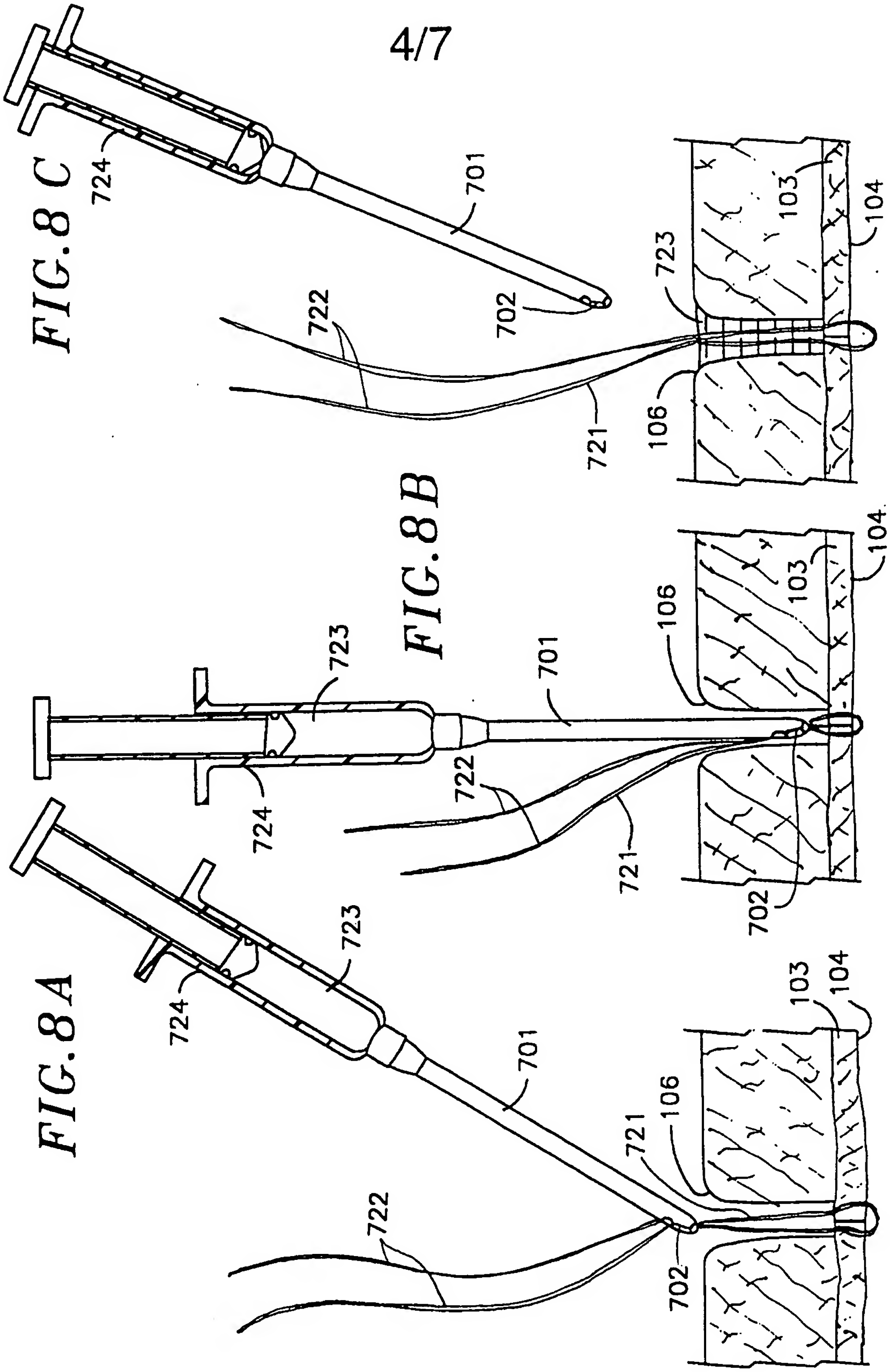

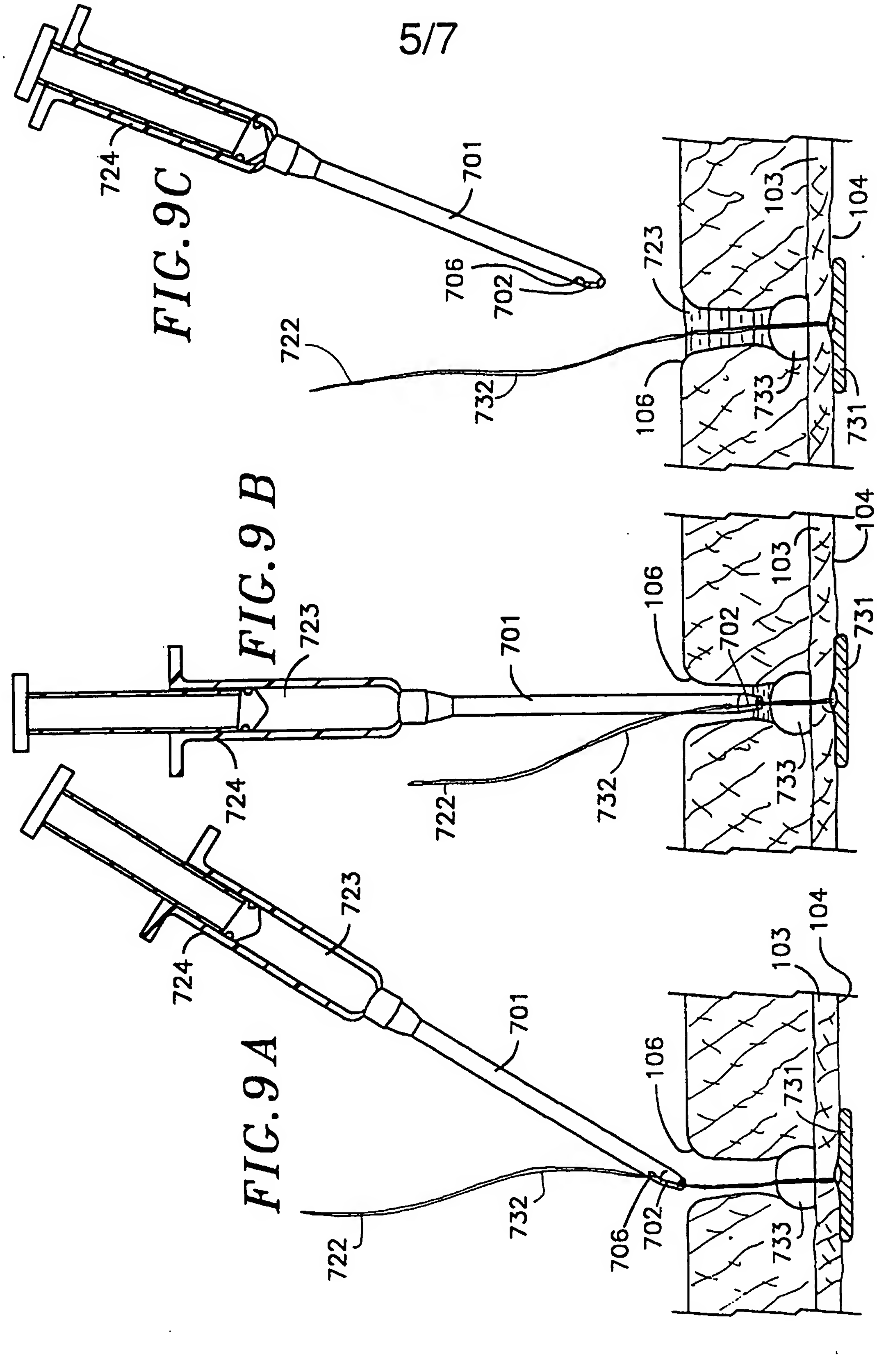

FIG. 9A

FIG. 9B

FIG. 9C

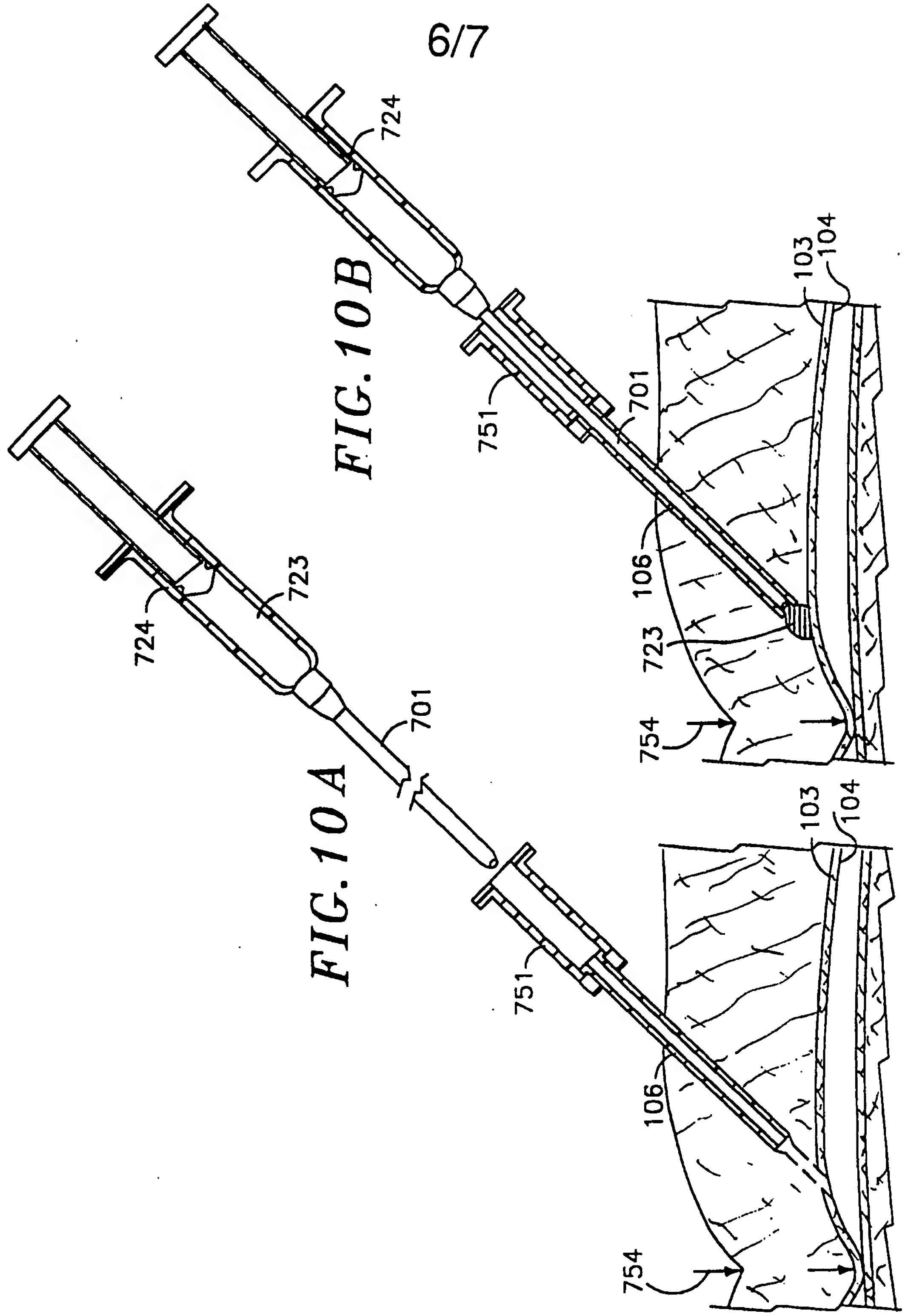

FIG. 10B

FIG. 10A

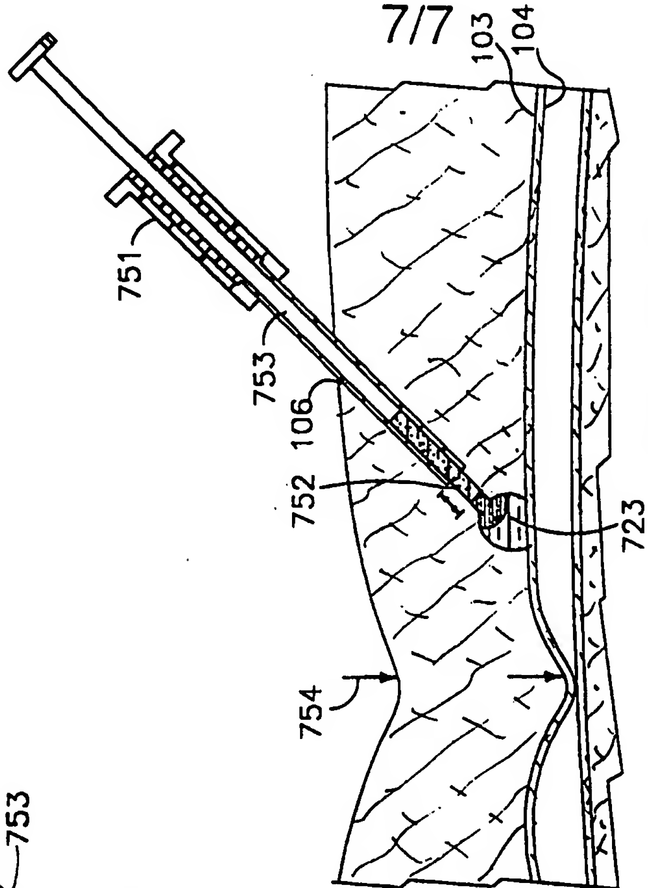

FIG. 10D

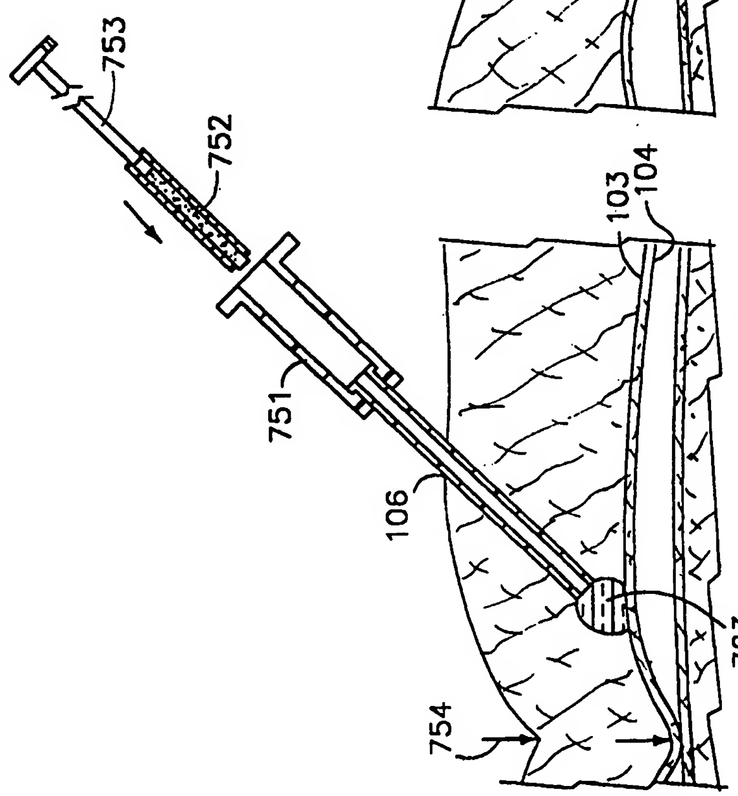

FIG. 10C

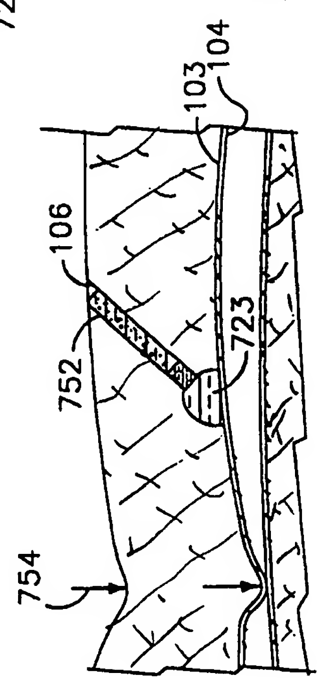

FIG. 10E

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/21744

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61B 17/00
US CL :606/213
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/213-216

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,290,552 A (SIERRA et al.) 01 March 1994, entire document.	1-7, 12-15

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search 22 NOVEMBER 1999	Date of mailing of the international search report 15 DEC 1999
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer VIKKI TRINH Telephone No. (703) 308-8238